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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/563,655

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J. Christopher Anderson

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

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ALAMEDA, CA 94501

EXAMINER

GEBREYESUS, KAGNEW H

ART UNIT

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1656

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/563,655	Applicant(s) ANDERSON ET AL.	
	Examiner KAGNEW H. GEBREYESUS	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/28/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response on September 18, 2008 to the Office Action dated June 16, 2008 is acknowledged. Applicants have amended claim 17 and 18-21, 25 and. Upon examination of newly added claims, it is deemed that this application now contains patentably distinct species of inventions that were not presented.

Newly added species are directed to invention that are distinct from the invention originally claimed for the following reasons: Claims 17-26 now include the O-tRNA species of SEQ ID NO: 1, 2, 4 and 5 which are drawn to patentably distinct subject matter. Since applicant has received an action on the merits for the originally presented species encompassing SEQ ID NO: 3, 6, 7 and 12 this invention has been constructively elected by original presentation for prosecution on the merits. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 17-26 comprising the ORS of SEQ ID NO: 15 and the O-tRNA species of SEQ ID NO: 6, 7 or 12 are present for examination.

All objections and rejections not reiterated from the previous Office Action are hereby withdrawn.

Maintained - Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-26 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue:

“...The amended forms of claims 17 and 26 now define the members of the genus of leucyl-O-tRNA molecules specifically by structural limitation, *i.e.*, a leucyl-O-tRNA comprising a nucleotide sequence selected from SEQ ID NOS: 1, 2, 4-7 and 12. Each of these members is defined in the specification; see the nucleotide sequences in Example 2 starting at paragraph 0218. Applicants assert that this amendment renders the rejection moot, and Applicants respectfully request that this rejection be withdrawn. Claim 19 was rejected under 35 U.S.C. § 112, first paragraph, where the specification allegedly lacks written description for "cognate synthetase," and therefore, a genus of O- tRNA/O-RS pairs that are "50% as effective" as a reference O-tRNA/O-RS pair cannot be readily determined...”

Applicant's argument has been carefully considered but not persuasive because the amendments to the claims do not overcome the lack of description of the claims for the following reasons:

Claims 17-26 are drawn to a cell comprising a translation system that comprises orthogonal the leucyl-tRNAs (O-tRNAs) comprising a nucleotide sequence selected from SEQ ID NO: 6, 7 and 12 and a genus of Leucyl-orthogonal tRNA synthetase (Leu-O-RS) with any structure (claim 17, 19-26) or the synthetase of SEQ ID NO: 15 and any conservative variant thereof (claims 18) that preferentially aminoacylates said leu-O-tRNAs with any amino acid.

Claim 19 is included in this rejection because it is only functionally defined *i.e.* cells comprising any O-tRNA and O-RS with at least “50% suppressor efficiency” compared to the efficiency of an ORS of SEQ ID NO: 15 or 16 and the OtRNA of anyone of SEQ ID NO: 1, 2, 4-7 or 12. However the specification does not teach any correlation between efficiency of suppression and structure of any O-RS/O-tRNA pair. Each orthogonal pair wherein the O-RS preferentially aminoacylates a corresponding O-tRNA must be determined empirically, and the

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art or the instant disclosure do not teach any common disclosed structure upon which one of skill in the art can rely to envision other species of O-RS/O-tRNA pairs within the genus. Thus applicants could not have been in possession of the genus of O-tRNA and O-RS broadly encompassed in the claims at the time the invention was claimed.

Furthermore, according to the definition in the specification, the term ‘conservative variant’ (claim 18) encompasses sequences with 50% identity to SEQ ID NO: 15. The specification does not teach a structure/function correlation for any **Leu-O-tRS** sequence with up to 50% variation while retaining any degree of suppressor efficiency. Thus the specification does not convey to the skilled artisan that Applicants were in possession of the claimed genus of Leu-ORS variants or cognate synthetases that can suppress a suppressor codon with at least 50% efficiency.

Given this lack of description of representative species for the genus of ORS/O-tRNA encompassed in the claims, the specification does not sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 17-19, 21, 22-26 are rejected under 35 U.S.C. 102(e) as being anticipated by US PAT 7,083,970 B2 Schultz et al. Schultz et al teach compositions comprising an orthogonal tRNA^{leu} derived from five different archael Leucyl tRNAs for which the anticodon was replaced with amber suppressor codons.. Among the O-tRNA^{leu} disclosed, the O-tRNA^{leu} of SEQ ID NO: 105 shows 100% identity to the O-tRNA^{leu} of SEQ ID NO: 4 in the instant application. Furthermore Schultz et al teach an O-tRNA sequence comprising SEQ ID NO: 3 that shows 100% sequence identity to SEQ ID NO: 5 in the instant application. Schultz et al teach an O-RS of SEQ ID NO: 65 which is identical to the O-RS of SEQ ID NO: 15 in the instant application. The O-tRNA^{leu} of Schultz et al were derived from *Halobacterium* sp. NRC-1 while the O-RS^{leu} was derived from *Methanobacterium thermoautotrophicum* to suppress the β -lactamase reporter gene comprising an amber codon in *E. coli* (see fig. 20 and fig. 21). Schultz et al teach compositions comprising the above ORS and O-tRNA wherein said composition can be in a cell (see column 9 lines 38-39 of Schultz et al). Claims 1-12 teach **cells** comprising ORS/OtRNA that incorporate various unnatural amino acids into a protein of interest. The limitation of 50% suppressor efficiency is fulfilled because the O-tRNA of SEQ ID NO: 105 and the ORS f SEQ ID NO: 65 would have 100% suppressor efficiency (because these sequences are identical to

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SEQ ID NO: 4 and SEQ ID NO: 15 respectively). Therefore claims 17-19, 21, 22-26 are anticipated.

The applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 17-26 are rejected under 35 U.S.C. 102(e) as being anticipated by WO/2002/085923 Schultz et al (in IDS). The specification and the claims (claims 1-7, 10 and 11) in Schultz et al teach a cell comprising an orthogonal tRNA that recognizes a selector codon in the presence of an ORS. Claim 10 in Schultz et al (WO/2002/085923) teaches an O-tRNA (SEQ ID NO: 3) that is 100% identical to the leu-O-tRNA of SEQ ID NO: 3. Furthermore claim 11 in (WO/2002/085923 Schultz et al) teaches an O-RS of SEQ ID NO: 65 that shows 100% identity to the leu-O-RS of SEQ ID NO: 15 claimed in instant claim 18. While the claims are not recited identically, the teachings in Schultz et al encompass cells comprising a genus of O-tRNA/O-RS pairs, and identical species of O-tRNA/O-RS pairs that are claimed in the instant application.

The applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

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inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

Claims 17-26 are rejected under 35 U.S.C. 102(e) as being anticipated by WO/2002/086075-A2 Schultz et al (in IDS). Schultz et al teach novel compositions comprising an orthogonal tRNA (O-tRNA), where the O-tRNA recognizes a selector codon and the O-tRNA is preferentially aminoacylated with a unnatural amino acid by an orthogonal aminoacyl-tRNA synthetase. The orthogonal tRNA-aminoacyl-tRNA-synthetase compositions are useful to incorporate unnatural amino acids in a polypeptide in vivo see for example claim 3 wherein the composition is optionally a cell see claim 36. Schultz et al teach the polynucleotide sequence of SEQ ID NO: 3 derived from *Halobacterium* NRC-1 T^{TG} tRNA which shows 100% sequence identity to SEQ ID NO: 4 in the instant application.

It should be noted that the previous Office Action stated that SEQ ID NO: 3 of Schultz et al (WO/2002/086075-A2) was 100% identical to SEQ ID NO: 3 in the instant application. Regardless of this inadvertent error, Applicant's SEQ ID NO: 3 was anticipated by SEQ ID NO: 2 of Schultz et al (WO/2002/086075-A2) that shows 100% identity to it.

Furthermore the O-RS of SEQ ID NO: 66 derived from *Methanobacterium thermoautotrophicum* is 100% identical to SEQ ID NO: 15 in the instant application. The functional properties of these orthogonal pairs (such as suppressor efficiency, aminoacylation etc) is inherent to the sequence of the molecule. Therefore claims 17-26 are anticipated by Schultz et al.

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The applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Conclusion:

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656
3/25/2009

/Andrew D Kosar/
Primary Examiner, Art Unit 1654